

FEATURED ACTIVITIES of DERT
October 2003

MEETINGS

Genes, Environment & Disease

June 7-9, 2003

Harvard School of Public Health and the Seaport Hotel
Boston, Massachusetts

Drs. Joan Packenham, Kimberly Gray, and Elizabeth Maull, SPHB, in conjunction with the Harvard Comparative Mouse Genomics Center, organized and convened a scientific symposium under the auspices of the Environmental Genome Project titled “Genes, Environment and Disease.” This meeting was held on June 7-9 in Boston, Massachusetts, at the Harvard School of Public Health and Seaport Hotel. The scientific symposium was designed to examine the role of genetic variation in gene-environment interactions, emerging technologies used in the study of genetic variation, and to examine issues of ethics and social consequences related to the discovery of environmentally responsive genes in human populations.

Symposium Goals

The mission of the Environmental Genome Project is “to improve the understanding of human genetic susceptibility to environmental exposures.” The goals of the year meeting were:

1. To review the state-of-the-art research relevant to gene-environment interactions and human genetic susceptibility, with a focus on the impact of these factors on human health and disease,
2. To foster dialog and discussion that may lead to new directions for the Environmental Genome Project,
3. To encourage and facilitate multidisciplinary discussion about issues related to studying genetic susceptibility of environmentally induced diseases in the laboratory setting and within human populations, and
4. To educate and inform scientists in all Environmental Genome Project-related disciplines about programs, resources, and future needs in order to facilitate new research initiatives.

Following the symposium on June 9, EGP scientists, invited experts and NIEHS program staff participated in a Roundtable Discussion, moderated by Drs. Packenham and Gray. The goals of this discussion session were:

1. To initiate and facilitate discussion between EGP scientists who study genetic susceptibility to environmentally-induced disease in mouse models and EGP molecular epidemiologists who study genetic susceptibility in human populations; and
2. To enhance current and plan future activities of the EGP.

Highlights and Summary:

The following four themes emerged during the roundtable discussion:

1. The size of the DNA sample set and number of candidate genes targeted for EGP resequencing;
2. The need for an ethnically defined DNA sample set;
3. The interface between human population-based molecular epidemiology and animal model-based molecular genetics;
4. Mechanisms to enhance progress in functional analysis of SNPs and/or molecular epidemiology.
 - Although consensus was not reached during this discussion, the majority of participants supported increasing the size of the sample set for EGP resequencing and to determine if the samples could be ethnically defined.
 - The discussants emphasized the importance of SNP validation and functional characterization of SNPs in the current set of candidate genes.
 - Methods development is the most prevalent concern in order to enhance the interface between molecular epidemiology in human populations and molecular genetics in animal models.
 - Mechanisms that promote data sharing and sample sharing, as well as high throughput inexpensive genotyping and resequencing technology would facilitate progress in molecular epidemiology.

Eighth International Congress on Toxic Combustion By-Products

June 16-19

Umea, Sweden

The goal of the Eighth International Congress on Toxic Combustion By-Products was to provide an international forum to discuss topics on the origins, fate, and health effects of combustion. This field has gained significant relevance to worldwide environmental policy, as risk-based programs increasingly rely on the ability of advanced scientific research to provide mechanistic, diagnostic, and analytical answers to complex problems concerning air toxic exposure. The meeting brought together industrial, governmental, and academic researchers involved in basic and applied

engineering technologies and in health-related research in order to both identify and resolve key issues.

Congress sessions included Organic Pollutants, Metals in Combustion, Thermal Waste Treatment, Ash Treatment, By-product Monitoring and Emission Control.

Meeting Highlights

The meeting (1) critically examined the impact of mechanistic/toxicological knowledge of combustion by-products on human and ecological systems; (2) identified processes and principles related to the exposure to combustion by-products; and (3) discussed the development and application of innovative engineering technologies to reduce the amount and/or toxicity of combustion by-products.

Research on toxic combustion by-products may be characterized by its complexity – that is the complexity of the number of agents, complexity of their interactions, complexity of their sources and origins, and complexity of their environmental fates. A number of recommendations have come from these international congresses, among them are:

- Advanced methods are needed for characterization of the bioavailability of particle-associated pollutants. Fine particles can act as effective delivery systems for toxic chemicals, but the bioavailability of the toxins depends upon the nature of their interaction with the particles. Advanced methods for characterizing the nature of association and binding of stable molecular as well as radical species with various types of particles are essential.
- Improved computational methods for modeling gas and particle properties are needed. Detailed reaction kinetic mechanisms of pollutant formation and fate require accurate thermochemical and reaction rate parameters.
- Rapid microarray techniques should be applied for assessing potential health impacts of individual pollutants and mixtures. The varied and complex products formed in combustion systems can potentially induce a variety of health impacts alone or in combination in a manner that has previously defied characterization. Application of the rapidly advancing field of microarray technology to screening for various biological endpoints of individual pollutants and mixtures should be used to address this poorly understood but critical component of environmental health
- Additional research should be conducted to increase our understanding of the composition, sources, and health impacts of ultrafine particles and nano-particles. Atmospheric studies should determine the composition of ultrafine particles, as well as nano-particles; determine the ratios of elemental carbon (EC) to organic carbon (OC) in airborne particulate matter; identify the main sources for ultrafine and nano-particles; and identify alterations of ultrafine and nano-particles by time and by location.

- Research in toxicology should be advanced to determine the fate of ultrafine particles and nanoparticles during inhalation and after deposition (dosimetry); determine translocation rates to other extrapulmonary tissues and influence of particle chemistry on such translocation; evaluate specific cellular and molecular mechanisms via both animal and *in vitro* studies; develop and use compromised animal models; and to apply toxicogenomics and proteomics in mechanistic studies.
- Concerted and focused efforts should be made to fulfill the potential of biomarkers to significantly reduce the burden of exposure and disease and to protect individuals from the uncertainty of risk, specifically in the area of exposure and effects of combustion by-products.

Dr. William Suk, CRIS, served on the organizing committee for the 8th International Congress. The 8th International Congress is directly related to ongoing research of NIEHS, primarily in the area of assessing and evaluating risk in humans and in research issues germane to chemical exposure from hazardous substances. It was supported, in part, by the Superfund Basic Research Program. Other co-sponsors included the U.S. Environmental Protection Agency, the Coalition for Responsible Waste Incineration, Louisiana State University, University of California, Berkeley, Umea University, and the United Nations Environment Programme.

The 9th International Congress on Combustion By-Products is scheduled for June, 2005, at the University of Arizona.

Metabolic Profiling: Application to Toxicology and Risk Reduction An International Conference

May 14-15, 2003

Research Triangle Park, North Carolina

The NIEHS/NIH/DHHS cosponsored an international conference on “Metabolic Profiling: Application to Toxicology and Risk Reduction” with the Office of Rare Diseases/NIH/DHHS, Food and Drug Administration, Paradigm Genetics and Waters Corporation. The meeting, held May 14-15 in Research Triangle Park, North Carolina, convened a multidisciplinary group of research and computational scientists from academia, industry and government to define the state of the science for the emerging area of metabolic profiling, also called metabonomics or metabolomics, and its application in basic and applied health research. The conference agenda and selected presentations can be found at <http://www.niehs.nih.gov/dert/metabol.htm>. A summary of the science of metabolomics as well as future research directions and challenges are summarized here. A full meeting report will be published later this year. *Dr. Brenda Weis, CRIS*, was the lead organizer of this meeting.

Metabolites are the end products of cellular processes and their levels reflect the integrated response of biological systems to genetic and environmental influences. Metabolic profiling is defined as a high throughput approach to measuring and interpreting the complex, time-related

concentration, activity and flux of endogenous metabolites in biosamples (urine, blood, tissues, cells).

- Metabolomics is a new word but not a new science. Studies aimed at measuring metabolites in biological systems have been ongoing for over 50 years with a long history of studies on intermediary metabolism. What is new is the ability to measure and quantify the full complement of metabolites in biosamples, thus, greatly enhancing our capability for scientific discovery. Integration of old and new studies is needed.
- The metabolome is an integral part of biological pathways and networks, “downstream” of the genome and the proteome and more directly influenced by external agents such as diet, drugs, disease, and chemicals. Integrated studies involving these complementary datasets are needed to construct models of how biological pathways, networks and systems function in producing toxicity and delivering health. This challenging task will require new databases and computational tools.
- The metabolome is complex, involving a range of small molecules (peptides, lipids, amino acids) with varying size, structure, polarity and function. There are several metabolomics technologies in use, including LC-MS/MS, NMR, FT-MS. More work is needed to evaluate and improve the sensitivity and specificity of these technologies for a variety of applications (blood, urine, cells, cellular compartments).
- There are ongoing efforts to link changes in metabolite profiles to histological changes in target organs and tissues. These studies should be expanded to include multiple time points and species, and to address normal variations in metabolites, in order to validate the use of metabolomics in predictive toxicology and risk assessment. Specific emphasis should be placed on describing the dynamics of metabolite activity and flux in biological systems.
- Metabolomics approaches are being applied to drug development, detection of adverse responses and disease diagnosis. Defining metabolite profiles in blood and urine samples has been used to classify the status and progression of metabolic disorders, diabetes, and neurodegenerative, renal and cardiovascular diseases. Additional studies are needed to define the underlying biological mechanisms in order to personalize clinical diagnosis, treatment and prevention.
- The field of metabonomics offers tremendous opportunities for environmental health research; however, relatively little work has been devoted to environmental or occupational exposures. NIEHS should take the lead and foster partnerships among federal agencies, academia and industry to advance the application to toxicology and disease risk reduction.

Embryonic Stem Cell Biomedicine: The Journey from Mice to Patients

May 15-17, 2003
University of Pittsburgh, Pittsburgh, Pennsylvania

Human Stem Cells (HSCs) and Human Embryonic Stem Cells (hESCs) have burst upon the biomedical/medical research scene like no other “breakthrough” advance in the health sciences in the last thirty years save one – whole animal cloning. The NIEHS has moved quickly to explore the potential of human stem cells for environmental health sciences research and environmental medicine applications. Unlike cloning, human HSCs bear a more immediate promise of new tools for research and new medical treatments for previously intractable human diseases and disorders.

Background

Dr. McClure, former Chief COSPB, organized a brainstorming session on November 18, 2002, to explore the potential in environmental health sciences research of embryonic stem cell research. Nearly two-thirds of the investigators leading major stem cell research programs attended. As an outcome, the NIEHS sponsored this international human embryonic stem cell research symposium. Dr. McClure co-organized the symposium with Dr. Gerald Schatten, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania. Dr. McClure introduced and moderated a session in the symposium, which also involved a number of NIEHS scientists. The symposium was held contiguous with the 1st Annual Human Embryonic Stem Cell Research Training Course funded by the OD, NIH. Dr. McClure served on the faculty for the training course. He also served on the organizing committee for the June 12, 2003 NIH Director's conference entitled "NIH Research: Recent Progress and Future Promise of Human Embryonic Stem Cells and moderated the introductory session on "stem cell plasticity." This conference followed contiguously with the First Annual meeting of the International Society for Stem Cell Research in Washington, D.C. as coordinated with the NIH Stem Cell Research Implementation Committee.

Research Recommendations

A number of research recommendations have come from the May 15-17 meeting, together with the other stem cell research meetings convened by or with the assistance of the NIEHS:

- The development of advanced methods for characterizing and validating HSCs and hESCs identities and potency is needed.
- Improved *in vitro* culture methods for HSCs or hESCs that will maintain their initial state of potency are needed. Additionally, reliable culture methods are needed that do not rely on animal/human cell feeder layers (prevent disease transmission risk) and predictably allow expansion of the parent cell populations.
- Research should be conducted to increase our understanding of the signaling molecules and mechanisms that communicate instructions guiding HSCs or hESCs into and through defined differentiation pathways leading to tissue-specific cell types. In particular, the role of genomic imprinting in regulating genomic gene networks associated with the progressive restriction of cell potential needs to be aggressively explored.

- The metabonomics and metabolonomics of stem cells differentiating into cell lineages needs to be actively studied *in vitro* to establish paradigms for translation to the *in vivo* circumstance of the progeny cell growth, regulation and life potential.
- Engraftment research must be aggressively pursued to identify and characterize the host individual's acceptance parameters that are required to ensure the integration of stem cell progeny into the target tissue or organ. The pathobiology of engraftment failure must be explored deeply due to the risk of adding morbidity or mortality factors instead of ameliorating existing ones.
- hESCs from donors bearing defined genetic mutation(s), single nucleotide polymorphisms (SNPs), or complex genetic disease traits offer huge potential for modeling the human health consequences of such inborn traits. Studies of these knock-outs, knock-ins, knock-downs, knock-ups, or silenced genes or gene networks) could be translated to knowledge of the human condition with the highest degree of direct relevance.
 - a. Comparative *in vitro* and *in vivo* effects of the allelic variations of the expression of such traits and how they contribute to genetic/epigenetic susceptibility to environmental toxicant or toxin exposure(s) should be thoroughly studied in *in vitro* stem cell models. This includes life-span animal model studies of host recipients derived from or bearing stem cell originated tissue/organ cell populations exposed to environmental agent or factor insult(s). Such studies of exposures to a toxicant or mixtures of toxicants could elucidate the consequences or predicted consequences of the related acute and chronic pathobiology to morbidity and mortality over the full lifespan of exposed individuals.
 - b. Engraftment integrates animal or human stem cells of defined function and lifespan parameters into the tissues or organs of recipient animal models. This offers the potential to study "built-in" susceptibilities to environmental agent or factor exposures in animals of defined genetic backgrounds or to "build-in" resistance to same. Such research could lead to high efficiency "alternative models" for research on the effects of toxicant exposures in environmental health and risk assessment. Further, such research could lead to regenerative medicine treatments using stem cell based tissue engineering for the treatment of individuals injured by incidental, occupational or military tissue/organ environmental agent toxicities.

DEFT PAPERS OF NOTE

Uracil Positioning Affects Efficiency of Base Excision Repair Enzymes

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R01ES04106

Background: DNA damage can occur from a wide variety of environmental agents including UV and other sources of ionizing radiation and cancer-causing chemicals. As a major defense against environmental damage to cells, DNA repair systems are present in organisms as diverse as bacteria, yeast, fruit flies, fish, amphibians, rodents and humans. DNA repair is involved in processes that minimize cell killing, mutations, DNA copying errors, and genomic instability. Abnormalities in repair processes have been implicated in cancer and aging.

Advance: Researchers at the University of Washington and the National Institute of Environmental Health Sciences report here that DNA repair enzymes do a much better job of repairing damaged DNA depending on whether the orientation of repair enzymes is toward or away from nucleosomes. Nucleosomes are complexes of chromatin material and chromosomal protein structures known as histones. Histones act as spools around which DNA winds, thus facilitating its compaction so that the large genomes of advanced animals will fit into every cell nucleus.

Implications: This novel finding represents a new model for studying DNA repair and opens new insights into the efficiency of repair processes. It also has implications in possible therapeutic treatments aimed at improving repair mechanisms to prevent and treat serious diseases associated with DNA repair abnormalities such as cancer and Alzheimer's.

Citation: Beard BC, Wilson SH, Smerdon MJ. Suppressed catalytic activity of base excision repair enzymes on rotationally positioned uracil in nucleosomes. Proc Natl Acad Sci U S A. 2003 Jun 24;100(13):7465-70. Epub 2003 Jun 10.

Sperm Abnormalities in Men Exposed to PCBs and PCDFs

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R01ES11256

Background: Polychlorinated biphenyls (PCBs) were used in transformers and other industrial applications because of their superior insulating properties and stability. When the adverse health effects of this class of compounds were discovered in the 1970s, they were banned by much of the world. However, because of their persistence, they are among the most ubiquitous man-made environmental contaminants and are detectable in most human beings worldwide. Polychlorinated dibenzofurans (PCDFs) are produced when PCBs are burned and are equally persistent and toxic.

There are many instances of accidental poisonings from exposure to PCBs. One such incident occurred during a six-month period in Taiwan in 1978-1979. The poisoning was traced back to contaminated cooking oil. PCBs had leaked from heat exchangers into the finished oil product. The PCBs were partially degraded by the heat, which produced PCDFs and other chlorinated multi-ring compounds. Approximately 2,000 people consumed the contaminated oil in what became known as the Yucheng or “poison oil” incident. A registry of those exposed was created to track adverse health outcomes.

A previous study of prenatally exposed young men born to Yucheng women showed increased abnormal sperm morphology, reduced motility, and reduced fertility; however effects of post-natal exposures to PCBs/PCDFs are less well documented. The study described below assessed the sperm quality of men directly exposed to PCBs and PCDFs in the Yucheng incident.

Advance: As in the previous study, directly exposed men exhibited higher abnormal sperm morphology than controls. A standard measure of fertility, the ability of sperm to penetrate hamster oocytes, was also lower in the directly exposed men, just as it was in the earlier study. Other semen characteristics were similar between exposed and control subjects.

Implications: This is the first study to show adverse effects in sperm from men directly exposed to PCBs and PCDFs. These findings are compatible with a previous study of prenatally exposed men and also with animal studies investigating similar compounds. The male-to-female offspring ratio was reduced in Yucheng men exposed before age 20 years. The current data suggest that the reduced capability of oocyte penetration found in this study may be specific to Y chromosome-bearing sperm, but this has not been confirmed and warrants further investigation.

Citation: Hsu PC, Huang W, Yao WJ, Wu MH, Guo YL, Lambert GH. Sperm changes in men exposed to polychlorinated biphenyls and dibenzofurans. JAMA. 2003 Jun 11;289(22):2943-4.

Birth Outcomes of Women Exposed to Dioxin in Seveso Italy

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R01ES07171 and P30ES01896

Background: On July 10, 1976, an explosion occurred at an chemical manufacturing facility in Seveso, Italy. Approximately 30 kg of dioxin were released into the environment resulting in the highest exposure to 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) known in human residential populations. Eleven communities in the densely populated area between Milan and Lake Como were contaminated. Researchers at the University of California Berkeley, along with colleagues in Italy at the University Milano-Bicocca, initiated the Seveso Women's Health Study to determine whether there was an association between TCDD exposure and adverse reproductive health outcomes.

TCDD is considered to be one of, if not the most toxic man-made substance. It has been shown to cause cancer and disrupt multiple endocrine functions. TCDD is a by-product of several manufacturing processes such as paper production and pesticide formulation. Among its varied effects, TCDD has been shown to cause increased fetal loss and reduced birth weight in animal studies.

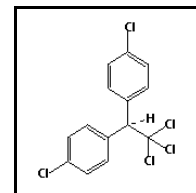
Advance: In the current study, the pregnancy outcomes of 510 women representing 888 total pregnancies were examined in relation to TCDD in serum samples collected from these women shortly after the explosion. Ninety-seven of the pregnancies ended in spontaneous abortions. There were no significant associations between TCDD exposure and spontaneous abortion, birth weight, or births that were small for gestational age. However, although not statistically significant, there were stronger associations for birth weight and small for gestational age among pregnancies that occurred within the first eight years after exposure.

Implications: This study reports the lack of a statistically significant association between maternal serum levels of TCDD and adverse birth outcomes in this cohort of women. However, the authors state "It remains possible that the effects of TCDD on birth outcomes are yet to be observed, because the most heavily exposed women were the youngest at follow-up and therefore are less likely to have yet had a post-explosion pregnancy." Additional epidemiologic studies are planned to further investigate this exposure.

Citation: Eskenazi B, Mocarelli P, Warner M, Chee WY, Gerthoux PM, Samuels S, Needham LL, Patterson DG Jr. Maternal serum dioxin levels and birth outcomes in women of Seveso, Italy. *Environ Health Perspect.* 2003 Jun;111(7):947-53.

DDT and DDE: Second Generation Time to Pregnancy Effects

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R01ES08345



Background: DDT was originally prepared in 1873, but it was not until 1939 that Paul Muller discovered the effectiveness of DDT as an insecticide. He was awarded the Nobel Prize in medicine and physiology in 1948 for this discovery.

The use of DDT increased enormously worldwide after World War II, primarily because of its effectiveness against the mosquito and lice. The World Health Organization estimates that during the period of its use approximately 25 million lives were saved predominantly from malaria and typhus. However, many species of insects developed resistance to DDT; it proved to have a high toxicity toward fish; and it was responsible for the near extinction of several bird species because of its interference with the formation of egg shells. For these reasons and because of its environmental persistence, the use of DDT was banned in the United States in 1972. However, It is still in use in some other parts of the world.

In mammals, DDT is of relatively low toxicity, but it does have troubling effects. DDT and its major metabolite, known as DDE, are persistent and are stored in fat tissue. DDT is known to have weak estrogenic activity and DDE has considerable anti-androgenic activity. They cross the placenta potentially interfering with fetal development. To further investigate possible effects on the human reproductive system, this team of investigators measured DDT and DDE levels in maternal serum samples collected from 1960-1963 in the Child Health and Development Studies. They compared these levels to the time to pregnancy in 289 daughters around 30 years later.

Advance: This is the first report to link DDT exposure in early life to human reproductive problems 30 years later. There was a clear association between increased DDT concentrations in maternal blood with a decreased chance of pregnancy in the daughters. For every 10 mg/L of DDT in maternal serum, the probability of pregnancy dropped 32%. However, quite unexpectedly, the chance of pregnancy increased 16% with each increase of 10 mg/L of DDE. The opposing effects of DDT and DDE may explain why large changes in reproductive performance have not been noticed in humans since the introduction of DDT.

Implications: Although the decreased fertility associated with *in utero* exposure to DDT remains unexplained, the authors speculate that the “antiandrogenic effects of DDE may mitigate harmful androgenic effects on the ovary during gestation and early life.” This study demonstrates the long delay from exposure to noticeable effect. The findings support both the establishment of new long-term human studies that can monitor effects of environmental exposures on reproduction as well as continued support of existing studies where multigenerational follow-up is in progress.

Citation: Cohn BA, Cirillo PM, Wolff MS, Schwingl PJ, Cohen RD, Sholtz RI, Ferrara A, Christianson RE, van den Berg BJ, Siiteri PK. DDT and DDE exposure in mothers and time to pregnancy in daughters. *Lancet*. 2003 Jun 28;361(9376):2205-6.

The Form of Vitamin E in Food Reduces Inflammation Triggers

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P01ES01896

Background: Chronic inflammation not only causes pain as in rheumatoid arthritis, it is also an important factor in fatal and disabling conditions such as asthma, hepatitis, diabetes, cancer, neurodegenerative disorders, cardiovascular disease, etc. Inflammatory responses are mediated by the production of compounds known as eicosanoids, which are derived from arachidonic acid. Prostaglandin E₂ (PGE₂), an eicosanoid produced by a cyclooxygenase-catalyzed oxidation reaction of arachidonic acid, is believed to cause pain and fever. PGE₂ and another oxidatively produced compound, leukotriene B₄ (LTB₄), and the enzymes that catalyze their production have been recognized as key targets for drug therapies in inflammation-associated diseases.

These researchers recently reported that g-tocopherol (gT), the major form of vitamin-E found in the U.S. diet, and its major metabolite inhibit the production of PGE₂. However, a-tocopherol (aT), the major form of vitamin-E found in tissues and in most vitamin supplements proved to be much less effective in this regard. The current study was performed to further investigate these effects in a mammalian model as opposed to an *in vitro* system.

Advance: Administration of gT, but not aT, to laboratory rats significantly reduced PGE₂ and LTB₄ synthesis. gT also significantly reduced the inflammation-mediated increase in a biomarker for lipid peroxidation. The inflammatory cytokine, tumor necrosis factor- α , was also reduced by gT.

Implication: This study shows the importance of gT in reducing the production of pro-inflammatory products and attenuated inflammation-mediated damage in a rat model. This observation, along with previous studies from this laboratory, strongly suggests that gT is important to human health and deserves further study. It also suggests that people suffering from inflammatory diseases might respond well to additional gT in their diet or from gT-containing supplements.

Citation: Jiang Q, Ames BN. Gamma-tocopherol, but not alpha-tocopherol, decreases proinflammatory eicosanoids and inflammation damage in rats. FASEB J. 2003 May;17(8):816-22.

Methylmercury Exposure from Ocean Fish Consumption and Neurodevelopment

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R01ES10219, R01ES08442, P30ES01247, and T32ES07371

Background: Exposure to methylmercury before birth has been shown to cause disruptions in neurobehavioral and cognitive development in children. The most common route of exposure is through maternal consumption of mercury-contaminated seafood products, but there have been conflicting reports on whether this level of exposure is harmful. NIEHS has funded two long-term studies on distinct populations of children in the Faeroe Islands and the Republic of Seychelles with distinctly different dietary exposures. The Faeroe Islanders consume whale meat while the Seychelle populations consumes only fish. The overriding question addressed by these studies is whether seafood consumption by pregnant and nursing women results in mercury exposures in their children at levels high enough to cause harm.

Advance: The study highlighted here was carried out in a population cohort, which consisted of 779 mother-infant pairs residing in the Republic of Seychelles. The mothers reported consuming 12 meals of fish per week. These fish contained about the same concentrations of methylmercury as commercial ocean fish found elsewhere. Only two endpoints were associated with prenatal methylmercury exposure. Increased exposure was associated with decreased performance in a standardized motor control test and improved scores in the hyperactivity index of the Conner's teacher rating scale.

Implication: These data do not support the hypothesis that there is a neurodevelopmental risk from prenatal methylmercury exposure resulting solely from maternal ocean fish consumption. An accompanying editorial by Dr. Constantine G Lyketsos of the Division of Geriatric Psychiatry and Neuropsychiatry at Johns Hopkins Hospital reaches the same conclusion. "On balance, the existing evidence suggests that methylmercury exposure from fish consumption during pregnancy, of the level seen in most parts of the world, does not have measurable cognitive or behavioral effects in later childhood." The editorial goes on to state that "the positive findings from the Faeroe Islands and New Zealand studies may be related to the fact that pilotwhale blubber and shark muscle contain 5–7 times the concentrations of methylmercury than the fish consumed in the Seychelles." Dr. Lyketsos' final conclusion is that "there is no reason for pregnant women to reduce fish consumption below current levels, which are probably safe."

Citation: Myers GJ, Davidson PW, Cox C, Shamlaye CF, Palumbo D, Cernichiari E, Sloane-Reeves J, Wilding GE, Kost J, Huang LS, Clarkson TW. Prenatal methylmercury exposure from ocean fish consumption in the Seychelles child development study. *Lancet*. 2003 May 17;361(9370):1686-92.

Exposure to Second-Hand Tobacco Smoke Increases School Absenteeism in Children

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P01ES09581 and P30ES07048

Background: Research has shown that exposure to environmental tobacco smoke (ETS) is responsible for respiratory illnesses among young children; however, the ETS-associated morbidity for school-age children is less well defined. Previous research by this team has shown that asthma-related school absenteeism is a major problem in southern California accounting for a large portion of all absences. To determine the extent to which ETS exposure might be implicated in school absenteeism, the team investigated the relations between ETS exposure, asthma status, and illness-related school absences in 1,932 fourth-grade schoolchildren from 12 southern California communities.

Advance: Overall, ETS exposure was associated with a 27% increased risk of respiratory-illness-related school absences. Children living in a household with two or more smokers were at a substantially higher risk (75%) of such absences. Children with asthma were at increased risk of respiratory-illness-related school absences. When exposed to one smoker, the risk was 2.35 times higher and when exposed to two or more smokers, the risk increased to 4.45.

Implications: This study demonstrates that ETS exposure is associated with increased respiratory-related school absenteeism among children with much higher risks for children with asthma. Approximately 9 million children in the U.S. suffer from asthma, which causes millions of lost work hours for parents who must stay home from work to care for them. This research shows that ETS plays a major part in some of these absences and points out the need for smoking cessation programs, especially for the parents of children with asthma.

Citation: Gilliland FD, Berhane K, Islam T, Wenten M, Rappaport E, Avol E, Gauderman WJ, McConnell R, Peters JM. Environmental tobacco smoke and absenteeism related to respiratory illness in schoolchildren. *Am J Epidemiol.* 2003 May 15;157(10):861-9.

Triplet Repeats in the Myotonic Dystrophy Gene

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R01ES11347

Background: A recent report by Richard Sinden of Texas A&M University (*J Mol Biol.* 326(4):1095-11) described an unusual trinucleotide repeat sequence in the gene for spinocerebellar ataxia type 10. Genes in normal individuals contain short lengths of trinucleotide repeats in which a combination of nucleotides, the building blocks of DNA, are repeated a number of times, usually less than 30. Eighteen human genetic diseases have been associated with expansion of the number of these repeats, sometimes numbering in the thousands. These diseases

often become increasingly severe and have earlier onsets in successive generations.

A new study, from a different research team at Texas A&M, sheds light on repeat expansions in the gene for Myotonic Dystrophy (DM). DM is the most common inherited neuromuscular disease in humans affecting one in 8,000 people worldwide.

Advance: This paper describes a model system in which repeats of the trinucleotide sequence CTG from the DM gene are deposited into an intron in one copy of a tandemly duplicated pair of *APRT* genes. Selecting for homologous recombination between the duplicated copies of the gene enables the examination of changes to the inserted CTG repeats in cells located nearby a recombination event. Long CTG repeats experienced large contractions and generated a high frequency of rearrangements. Replicating cells displayed a high frequency of expansions and contractions that usually involve a small number of triplets. The results demonstrate that homologous recombination destabilizes long CTG repeats in this cell system.

Implication: The roles of contraction and rearrangements of trinucleotide repeat sequences, along with other aspects of DNA metabolism, in the development of triplet repeat diseases is unclear. This model offers insights on the mechanism of repeat expansion and may lead to further discoveries on how to prevent or repair these genetic defects. Scientists have theorized that if the cause of the repeat expansion can be discovered, there is hope in preventing them from occurring.

Citation: Meservy JL, Sargent RG, Iyer RR, Chan F, McKenzie GJ, Wells RD, Wilson JH. Long CTG tracts from the myotonic dystrophy gene induce deletions and rearrangements during recombination at the *APRT* locus in CHO cells. *Mol Cell Biol.* 2003 May;23(9):3152-62.

Hydrogen Peroxide: A Messenger Important in Cancer Cell Survival

P. Andrew Karplus, Ph.D., Department of Biochemistry and Biophysics, Oregon State University P30ES00210 (Joseph Beckman, Ph.D., Director)

Background: Hydrogen peroxide, known mostly as a common antiseptic, is also a product of aerobic metabolism. As an organism consumes oxygen, small amounts of hydrogen peroxide are formed as a by-product. All aerobic organisms have evolved systems to control this simple molecule so that it doesn't accumulate in quantities sufficient to kill or damage cells. One such mechanism is the enzyme peroxiredoxin. Peroxiredoxin and other enzymes, such as catalase, act to destroy hydrogen peroxide. The story might end there, but there is a growing body of evidence that hydrogen peroxide is important for cell signaling and communication. A team of researchers, using support from the NIEHS Center at Oregon State University, has discovered that differences in the bacterial and human forms of peroxiredoxin affect how well it functions. These findings suggest that the enzyme plays a role in cancer development.

Advance: The team showed that the human enzyme is over 100 times more sensitive to damage by hydrogen peroxide than is the bacterial enzyme, and they revealed the structural explanation of this difference. They postulated that this must have evolutionary value; that perhaps the human peroxiredoxin acts like a “floodgate” keeping resting levels in control, but allowing higher levels to signal the cell to undergo programmed cell death.

Implication: What started as a basic research investigation into the function of the enzyme turned out to have implications for cancer therapy. Some cancer drugs, such as cisplatin used in testicular cancer, cause an increase in the production of hydrogen peroxide killing the cells from the inside out. Cancer cells that are resistant to cisplatin or other cancer therapies such as radiation, seem to be making larger amounts of peroxiredoxin which degrades the hydrogen peroxide before it has a chance to kill the cell.

Citation: Wood ZA, Poole LB, Karplus PA. Peroxiredoxin evolution and the regulation of hydrogen peroxide signaling. *Science*. 2003 Apr 25;300(5619):650-3.

Semen Quality Lower in Men from Rural Areas

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R01ES09916

Background: Many studies conducted over the last decade have reported large differences in semen quality parameters in men from different areas of the U.S. and in international studies as well. Comparisons of these studies are difficult because semen analyses are highly sensitive to the methods of semen collection and analysis. There are also indications that sperm concentrations declined dramatically during the 20th century; however, analytical differences again may be at least partially responsible for the decline.

In 1998, NIEHS funded the Study for Future Families, a multi-center study similar in design to multi-center studies being conducted collaboratively in Europe and Japan. The study’s goal is to estimate the geographic variability of semen parameters in men in the U.S. and to compare the results to those from other centers worldwide. A NIEHS-supported researcher at the University of Missouri, Columbia, the coordinating center for the U.S. study, recently reported the results of analyses from men in four distinct geographic areas.

Advance: The team studied 512 men in four areas: Columbia, Missouri; Los Angeles, California; New York, New York; and Minneapolis, Minnesota. Sperm concentration and the total number of motile sperm were significantly lower for men from Columbia, Missouri than the other three centers. Total motile sperm was 58% lower in the Missouri men than the men from Minnesota. Although some of the men had low semen quality, it was not low enough to cause infertility, since the men were partners of pregnant women.

Implication: A possible reason for these differences could be higher exposure to pesticides in the more rural Missouri population than the other areas. Fifty-seven percent of the land in the Columbia area is used for farming which far exceeds that of the other areas. Many animal studies have shown that pesticides affect fertility; however, more research is needed to determine if this is the cause for the differences seen in this study. Additional research is being planned in Iowa City, Iowa, an area with even higher exposure to pesticides than Columbia.

Citation: Swan SH, Brazil C, Drobnis EZ, Liu F, Kruse RL, Hatch M, Redmon JB, Wang C, Overstreet JW, The Study For Future Families Research Group. Geographic differences in semen quality of fertile U.S. Males. Environ Health Perspect. 2003 Apr;111(4):414-20.

Inhibition of IKK and NF- κ B Prevents Inflammation but Increases Local Injury

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P42ES10337

Background: NF κ B is a transcription factor that is a major regulator of immune responses stimulated by pro-inflammatory agents such as tumor necrosis factor, viruses, interleukin-1, and bacteria. NF κ B normally resides in the cytoplasm bound by an inhibitory protein known as I κ B. Phosphorylation of I κ B by I κ B kinase-b (IKK-b) releases NF κ B, which then moves into the nucleus where it acts in the induction of numerous regulatory genes of the immune system. The products of these genes are pro-inflammatory factors.

This paper describes the role of NF κ B in severe systemic inflammation and multiple organ dysfunction syndrome (MODS). MODS, a serious and often fatal condition, occurs in patients with septic and toxic shock and other systemic inflammatory response syndromes. Since activated nuclear NF κ B is often found at sites of inflammation and infection, it is thought to be a key mediator of both acute and chronic inflammatory diseases such as septic shock and asthma. In MODS, activated neutrophils infiltrate tissues resulting in the release of proteases, reactive oxygen species and various cytokines and inflammatory mediators that contribute to tissue injury and failure. NF κ B has been proposed as an important contributor in amplifying this response, but it is unclear whether it is crucial for initiating the inflammatory response.

Advance: Using a classic model to induce severe inflammation called gut ischemia-reperfusion in which the blood supply is cut off to the gastrointestinal tract for 30 minutes and then restored, these investigators determined that mice whose intestinal cells lacked IKK-b did not produce the predicted systemic inflammatory response. IKK-b works as a complex with two other proteins to allow activation of NF κ B following infection. However, the lack of IKK-b caused severe damage to the reperfused intestinal mucosa in these mice because of apoptosis or programmed cell death. Therefore, therapeutically blocking the activity of IKK-b in humans would likely block the inflammatory response, preventing MODS. However, this would occur at the cost of severe tissue injury caused by programmed cell death. These results show the dual roles for the NF κ B

system in both tissue protection and systemic inflammation.

Implication: This paper identifies two points that are important regarding future development and possible therapeutic use of IKK and NFkB inhibitors as anti-inflammatory agents. First, it provides “unequivocal and direct proof that NFkB is not just a marker of inflammation, but is the driving force for initiation and spread of acute and systemic inflammation.” Second is “ a primary role for NFkB activation in response to physical and chemical stressors is to protect the challenged cells or tissues from apoptosis.” Although IKK-b and NFkB inhibitors are likely to be potent anti-inflammatory agents, this study underscores the potential danger of using them during severe inflammatory episodes caused by shock, trauma, and other critical illnesses.

Citation: Chen LW, Egan L, Li ZW, Greten FR, Kagnoff MF, Karin M. The two faces of IKK and NF-kappaB inhibition: prevention of systemic inflammation but increased local injury following intestinal ischemia-reperfusion. Nat Med. 2003 Apr 7.

Low Levels of Lead and IQ Deficits

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R01ES08388 and P30ES01247

Background: Among environmental hazards, lead is one of the most prevalent and dangerous to children. Lead poisoning was first recognized and describes as a distinct entity 100 years ago. Since then, numerous studies have shown that blood lead concentrations above 10 micrograms/deciliter (mg/dl) are associated with adverse outcomes on intellectual development, functioning and behavior. Much of this work was supported by NIEHS and led the Centers for Disease Control and Prevention (CDC) in 1991 to set the “level of concern” for lead at 10 mg/dl. Very little data exists documenting adverse effects at concentrations below this level; however, the CDC and the World Health Organization do not recognize a threshold for lead associated deficits.

Advance: In a 5-year study of 172 children, a team of NIEHS-supported researchers from the University of Rochester, Cincinnati Children’s Hospital Medical Center, and Cornell University found that lead does cause intellectual impairment at low levels. The researchers found that IQ scores for children with blood lead levels at 10 mg/dl were about 7.4 points lower than for children at 1 mg/dl. Surprisingly, the study also concluded that as blood lead increased from 10 to 30 mg/dl, there was a more modest decline in IQ scores indicating that more damage occurs at lower levels for any given exposure.

Implication: The average blood lead level of children in the U.S. has been declining steadily since the removal of lead from gasoline and household paint. However, this study suggests that many more children--perhaps more than 1 out of 10--are affected by lead than previously

estimated. These data emphasize the importance of prevention and add further evidence that there is indeed no safe level of lead exposure.

Citation: Canfield RL, Henderson CR Jr, Cory-Slechta DA, Cox C, Jusko TA, Lanphear BP. Intellectual impairment in children with blood lead concentrations below 10 micrograms per deciliter. N Engl J Med. 2003 Apr 17;348(16):1517-26.

GRANTEE HONORS and AWARDS

James M. Tiedje, PhD., Michigan State University, has been elected to the National Academy of Sciences (NAS) in the scientific discipline of Environmental Sciences and Ecology. Dr. Tiedje is a current grantee of the Superfund Basic Research Program (SBRP) within Michigan State University's Project. His research is focused on understanding the ecology, physiology and molecular biology of microbial processes important in nature, including those that degrade environmental pollutants. According to the NAS, "In addition to fundamental contributions to the microbial ecology of biodegradation of anthropogenic compounds and of the nitrogen cycle, Tiedje has pioneered the use of molecular techniques to understand the nature and significance of microbial diversity in soils and sediments. He is the world's leading environmental microbiologist." Dr. Tiedje has also been elected as the incoming American Society for Microbiology's (ASM) President-Elect. He has been active in the ASM for many years, including service as Editor-in-Chief of *Applied and Environmental Microbiology* and was the recipient of its Environmental and Distinguished Service Awards. The ASM originated in 1899, and is considered the "oldest and largest life science membership organization in the world" with over 42,000 members. The ASM promotes the study of microbiological research and science and "their applications to the common good."

Bruce Weir, Ph.D., William Neal Reynolds Professor of statistics and genetics at North Carolina State University and one of the world's foremost researchers on statistical analysis of DNA for forensic, human health, and agricultural applications, was honored May 9 with the O. Max Gardner Award, the highest faculty award presented by the Board of Governors of the University of North Carolina.

STAFF HONORS and AWARDS

Dr. William Suk, was honored by the University of Cincinnati, with the *Roy E. Albert Memorial Award for Translational Research in Environmental Health*. The award was conferred at a workshop entitled "State Environmental and Health Agencies: Surviving in the Post 9/11 World", which was held at the Kingsgate Conference Center in Cincinnati, June 9. This award recognizes the efforts of those who have made major contributions to the advancement of science at the

interface between basic research in environmental health and practical applications to preventive medicine and/or public policy. An awardee may have had an outstanding career in research at this interface, or may have worked in an academic or governmental institution to promote outstanding research at this interface. The award was given to Dr. Suk for his work “fostering outstanding research at the interface of basic science, remediation of environmental contaminants, and public policy.”

The following awards were made at the Grants Management Awards Ceremony, held Friday, June 6 in Gaithersburg, Maryland.

Ms. Dorothy Duke, GMB, received an Excellence in Leadership Award for her commitment and leadership as co-chair of the GMAC Vision Steering Committee (VSC) for the second, one year term. In this capacity she has served as organizer and facilitator of the monthly VSC meetings and has continuously provided leadership and direction to the Committee as a whole as well as its individual members. She maintained the VSC membership and GM Infonet database based on the new membership structure adopted August 2001. She initiated and organized a Principals only GMAC and VSC combined meeting on December 18, 2002. This meeting was devoted to the review and evaluation of the missions and functions of the VSC and its subcommittees. The meeting was productive and brought new insights and recommendations for future directions to the VSC.

Ms. Carolyn Mason, GMB, received from the Vision Steering Committee a Special Recognition Award for outstanding contributions to the IMPAC II GM Lead Users Group and the Grants Management community for participation in the GM Module Edit Checks Working Group. The Edit Checks Working Group analyzed every GM Module edit check/business rule, recommended deletion of outdated edit checks/business rules and edited the wording of all warnings and errors. The efforts of the Edit Checks Working Group will simplify the use of the GM Module for all staff and will eliminate the need to analyze the edit checks/business rules when the GM Module is redesigned in FY2004.

Ms. Jackie Russell, retired from GMB, has received a Letter of Appreciation from the Vision Steering Committee for significant contributions to Compliance Education & Review Team activities and participation in the majority of subcommittee meetings during the past year.

Ms. Lerlita Garcia, GMB, has received a Letter of Appreciation from the Vision Steering Committee for significant contributions to Grant Expert Subcommittee activities and participation in the majority of subcommittee meetings during the past year.

STAFF ACTIVITIES

Dr. Van Houten, PAB, was a co-chair and invited speaker at the Gordon Research Conference on Genetic Toxicology, held in Oxford, United Kingdom, August 10-15. The title of his talk was "Oxidative Stress-Induced Mitochondrial DNA Damage: Sorting Out Life and Death Decisions."

Mr. Outwater, OD/WETB, assisted the U.S. Department of HUD as a reviewer for their 2003 Healthy Homes Demonstration Project awards through a series of a training period and conference calls. The final review meeting was held on August 6. *Dr. Srinivasan, SPHB*, worked in collaboration with Mr. Outwater.

Ms. Beard, OD/WETB, presented at the U.S. EPA Superfund Community Involvement Coordinators Conference on July 21 in Philadelphia, PA. The presentation was entitled "Keeping it Local: Engaging Community Based Organizations in Workforce Development Programs." WETP grantees Mark Holdbrooks and Kiameesha Evans from the University of Medicine & Dentistry of New Jersey and Donna McDaniels of the Laborers-AGC Education & Training Program also presented the accomplishments of our Superfund Jobs Training Initiatives as well as Brownfields and Minority Worker Training Programs to the coordinators.

Dr. McClure, COSPB, participated in the organizing of the 36th annual program for the Society for the Study of Reproduction (SSR) held July 19-22 in Cincinnati, OH. The meeting was supported in part by NIEHS funding for the theme of "Reproduction and the Environment," which included sponsored sessions for the President's Symposium (Reproduction and the Environment), a State of the Art Lectureship, three mini-symposia (Endangered Species and Reproduction, Endocrine Disruptors, Fetal Basis of Adult Disease) and the Trainee and Minority Affairs Forum on Career Development and Networking. At this meeting, the Board of Directors of the SSR formally approved the recommendation of the membership to establish the SSR Committee on Reproduction and the Environment (CoRE) populated by SSR members from the community of private sector, USDA, EPA, NIEHS, and NIOSH scientists. The CoRE sponsored an information booth at this meeting which was both well-visited and exhausted of hand-out materials within its first four hours. The purpose of the CoRE is to bring together reproductive and developmental biologists, toxicologists, and ecologists and promote greater collaborative, multi-disciplinary environmental health sciences research to improve the public health.

NIEHS hosted a Roundtable on Preparation and Protection of Site Disaster Responders in Beckley, WV on July 9. *Dr. Olden, Director, Mr. Hughes, Ms. Beard, and Mr. Outwater, OD/WETB* joined approximately 25 other participants from unions, universities, and other federal agencies to discuss further steps that are needed to adequately train workers who respond to disasters. The Roundtable included a demonstration of the coordinated efforts of emergency medical personnel, police, hazmat experts, and heavy equipment operators to deal with a simulated leak of a chemical from a tank truck and recovery of a victim incapacitated by the leak. Participants concluded that more detailed action plans are needed to determine the specific roles

and activation of emergency responders including skilled support personnel when responding to disasters. In addition, a pilot should be developed to test the use of a registry of responders.

Dr. Reinlib, SPHB, was an invited speaker to the "Workshop on Breast Cancer and the Environment" organized by the DHHS Office of Women's Health in Washington, DC on June 26. His presentation was entitled, "Breast Cancer Research Opportunities at NIEHS." The Workshop discussed the findings of major international studies on breast cancer and made recommendations for future directions for research that would better include stakeholders and for utilization of the resources of the Department's Centers of Excellence.

Dr. Van Houten, PAB, was a discussion leader for the "Introduction to Toxicogenomics" session at the Gordon Research Conference on Toxicogenomics, which was held June 22-27 in Lewiston, Maine.

Mr. Outwater, OD/WETB, gave an overview of the NIEHS Worker Education and Training Program to the Knight Journalism/CDC Boot Camp participants in Atlanta, GA on June 21. This was part of a collaborative activity with the Center for Disease Control and the International Association of Firefighters, an outstanding NIEHS awardee, to provide "awareness level" training for professional journalists designed to assist them in protecting themselves during hazardous materials and weapons of mass destruction incidents.

Dr. McClure, COSPB, served on the organizing committee for the June 12 NIH Director's conference entitled "NIH Research: Recent Progress and Future Promise of Human Embryonic Stem Cells," which was held at the main NIH campus in Bethesda, Maryland. The audience exceeded 800; the meeting was also televised live to two satellite sites at NIH and presented live on the NIH web-cast resource. Dr. McClure moderated the introductory session on "stem cell plasticity." This conference followed contiguously with the First Annual meeting of the International Society for Stem Cell Research in Washington, D.C. coordinated by the NIH Stem Cell Research Implementation Committee, upon which Dr. McClure serves by appointment of the OD, NIH.

Dr. Van Houten, PAB, was an invited speaker June 3 at the University of New York, Pharmacological Sciences Department, Stony Brook, New York where he gave a talk was entitled, "Arsenic, Oxidative Stress and Mitochondrial Damage: Sorting out Life and Death Decisions."

Dr. Mastin, COSPB, was an invited speaker at a sessions at the meeting of the American Thoracic Society, entitled, "Air Pollution as a Cause of Childhood Asthma and Chronic Airway Disease" on May 21. The purpose of the session was to present and discuss evidence for causative link between air pollution and childhood lung disease, primarily asthma, and to discuss areas for future research.

Ms. Beard, OD/WETB, hosted a Brownfields Focus Meeting in Research Triangle Park, North Carolina on May 20. This meeting focused on strengthening and promoting our strategic plan for Brownfields issues in 2003. All NIEHS/WETP Brownfields Minority Worker Training Awardees participated in this meeting. Staff attending and participating in the meeting included *Mr. Hughes, Mr. Outwater, and Ms. Thompson, OD/WETB*.

Dr. McClure, COSPB, delivered the introductory lecture to the class of 2003-2004 on May 17th and served on the faculty of the 6th Annual Frontiers in Reproduction (FIR) training course at the Marine Biological Laboratory (MBL) in Woods Hole, Massachusetts. He received an award acknowledging his leadership in founding and developing the FIR course. The course includes environmental health sciences faculty investigators and topics related to reproductive and developmental toxicology. From the international competition for the sixteen trainee positions available each year, one to two are awarded to young environmental sciences investigators actively engaged in developing a research career. Many of the environmental sciences investigator faculty and graduate trainees of FIR have become active members of other professional societies reproductive and developmental committees/activities promoting greater collaboration amongst the toxicology and biology community of scientists.

Dr. McClure, COSPB, served on the organizing committee for the 51st Annual Meeting of the Society for Gynecologic Investigation (SGI), which has the theme of "Genes, Cells and the Environment: Implications for Women's Health" and a post-graduate Course on "Epigenetic Regulation of Reproductive Development and Function: More than Just Genes. A substantial representation of speakers on these themes are NIEHS funded investigators. The meeting and post-graduate course will be held in Houston, Texas on March 24-27, 2004.

Drs. Sassaman (OD) and Suk (CRIS) hosted a delegation from the Vietnamese National Center for Science and Technology at NIEHS on September 2 and Dr. Sassaman with EPA in Washington, DC on September 3. The purpose of the visit was to continue to develop collaborations under a Memorandum of Understanding between the US and Vietnamese governments and to plan for a workshop to be held in Hanoi on remediation and exposure measurements November 3-5.

UPCOMING MEETINGS and WORKSHOPS

Mr. Hughes, OD/WETB, will address a study tour group from South Africa on the NIEHS Worker Education and Training Program. Hazardous in Washington, DC on September 20. The Development Associates, Inc. has been awarded a contract by the U.S. Agency for International Development (USAID) to provide technical services to the South African Department of Labour (DOL) and supporting government institutions. This major effort revolves around the passage of the Skills Development Act in 1998, which introduced a new approach to the promotion and development of work-related skills in South Africa.

Mr. Hughes, OD/WETB, will present at the EPA Emergency Support Function #10 Coordination for National Hazmat Disasters Committee in Washington, DC on September 24.

Ms. Beard and Mr. Outwater, OD/WETB, will attend the Brownfields 2003: Growing a Greener America Conference in Portland, Oregon on October 26. This national conference will build upon past successes and continue to offer up-to-date and stimulating information for brownfields practitioners from throughout the United States and overseas. The NIEHS WETP is a co-sponsor for this conference and several sessions will focus on brownfields job training, public health and environmental justice efforts of our grantee community. During this meeting, *Ms. Beard and Mr. Outwater* are also planning to conduct a grantee meeting of the Brownfields Minority Worker Training Program and a caucus meeting of those attendees interested in environmental job training programs. This caucus meeting is a collaborative effort between the WETP and Lenny Siegel of the Center for Public Environmental Oversight, who has conducted these very successful caucuses since 1996 at each Brownfields National Conference.

The conference "Emerging Scientific Issues for Superfund" will be held October 8 - 10 at the University of California, Berkeley. This conference will bring four current west coast Superfund Basic Research Program grantees together with their EPA Region 9 colleagues to examine emerging scientific issues for the Superfund Program including "Emerging Contaminants - New Threats," "Emerging Issues in Transport and Detection," and "Emerging Issues in Remediation and Treatment."

The Sero Symposia International (SSI) Workshop entitled "The Role of Environmental Factors on the Onset and Progression of Puberty" to be held November 6-8, 2003 at the Hyatt Regency O'Hare in Rosemont, Illinois. The workshop, sponsored by the SSI with the assistance of NIEHS, CDC and EPA will explore the extant body of knowledge to determine if a consensus can be reached with regard to the sufficiency of the data to support a secular trend in the age of puberty onset and progression in boys and girls and a role of the environment in influencing any such trend. *Dr. McClure, COSPB*, participated in the organizational planning of the workshop.

The annual meeting of the Superfund Basic Research Program (SBRP) grantees will be held November 9-12 at Dartmouth College in Hanover, New Hampshire. Throughout the three-day conference, technical sessions and presentations will highlight a broad spectrum of research, providing a greater understanding of the work currently being performed by the program's researchers. In addition to the conference's technical and student poster sessions, Administrators and Outreach Core staff from each SBRP university program will meet concurrently in their own meetings to review information relevant to their roles and responsibilities.

Mr. Hughes, OD/WETB, and staff will host the NIEHS/Worker Education and Training Program (WETP) semi-annual awardee meeting and technical workshop in Research Triangle Park, North Carolina, on December 3. The focus of the meeting is to take an inward look at the training, administrative core, and future directions of the WETP. Staff attending and participating in the meeting/workshop in various activities will include *Ms. Beard, Mr. Outwater, Ms. Thompson, OD/WETP, and Ms. Mason, GMB*.

STAFF CHANGES

Recruitments:

Dr. Gwen Collman became Chief of the Susceptibility and Population Health Branch in July. She earned a B.S. in Biology from State University of New York at Binghamton, an M.P.H. in Epidemiology from the University of Michigan, and a Ph.D. in Environmental Epidemiology, from the University of North Carolina School of Public Health. She has worked at the National Institute of Environmental Health Sciences since 1984, first as a member of the Epidemiology Branch in the Division of Intramural Research, and since 1992 as a member of the Chemical Exposures and Molecular Biology Branch, DERT. As a Scientific Program Administrator she was responsible for the grant portfolio in Environmental and Molecular Epidemiology. She was also responsible for developing and managing the NIEHS Breast Cancer and the Environment Research Program and the NIEHS/EPA Centers for Children's Environmental Health and Disease Prevention. In her new capacity, Dr. Collman is also the Program Director for the NIEHS Environmental Health Sciences Centers program.

Dr. J. Patrick Mastin has been named Chief of the Cellular, Organ and Systems Pathophysiology Branch. He received a B.S. degree in Biochemistry and Molecular Biology from Centre College in Kentucky and a Ph.D. in Pathology from Duke University. Prior to joining the NIEHS, Dr. Mastin was a Research Biologist and then Chief of the Immunochemistry Research Section at NIOSH. He joined DERT in July 1998, as a Scientific Review Administrator in the Scientific Review Branch. On May 16, 2001, he transferred to the Cellular, Organs & Systems Pathobiology Branch (Formerly OSTB) as a Program Administrator for the extramural Pulmonary, Cardiovascular Immunotoxicology, and Renal programs.

Dr. David Balshaw has recently joined The Center for Risk and Integrated Sciences as a Program Administrator, where he will be responsible for developing a portfolio in proteomics and systems biology. He comes to the Institute from the NHLBI where he served for two years as a program administrator, overseeing portfolios in ischemic heart disease and traumatic injury, and developing initiatives intended to facilitate the translation of basic research findings into clinical investigation and application. He was also one of the principal players in developing the NHLBI's Proteomics Initiative, a significant investment in technology development geared towards biological application. Dr. Balshaw earned his Ph.D. in the Department of Pharmacology and Cellular Biophysics at the University of Cincinnati where he focused on kinetic modeling of ion transport processes. Following his doctoral work, he took a fellowship at the University of North Carolina at Chapel Hill investigating the regulation of intracellular calcium release. His expertise includes protein biochemistry, molecular biology, and computational approaches to modeling biological phenomenon.

Ms. Lisa Archer has moved within DERT to a Grants Management Specialist position within the Grants Management Branch. Lisa has worked in DERT for all but three of her 12-year government career, most recently serving as an Extramural Information Specialist in the OD's office.

Ms. Pam Evans has joined the DERT as a Grants Management Specialist. Prior to joining DERT, she worked for three years as a Contract Specialist in the NIEHS Acquisitions Management

Branch. She has been employed with the government for more than 22 years. Prior to coming to NIEHS, she worked in procurement for the Departments of Defense and Veterans Affairs.

Dr. Ethel Jackson, who served as Chief of the Scientific Review Branch for many years, has relocated to the Office of the Director, where she is a Special Assistant to Dr. Sassaman and will direct staff training efforts, among other projects.

Dr. Dennis Lang, Deputy Director DERT, has been named Acting Chief of the Scientific Review Branch. Recruitment for a permanent branch chief will take place this fall.

Departures:

Dr. Michael McClure, Chief of the Cellular, Organ and Systems Pathobiology Branch retired on August 30, 2003 after 24 years of government service. Dr. McClure had been active in developing programs in reproduction at the National Institute of Child Health and Human Development before coming to NIEHS as branch chief with primary responsibility for program development in female reproductive toxicology. He was active in many trans-NIH issues and was instrumental in developing the first non-governmental joint program, that between the NIEHS and the American Chemistry Council on developmental toxicology.

Ms. Jackie Russell retired from GMB on May 31 after more than 30 years of government service.

Dr. Larry Reed, an EPA employee who has served as a guest researcher with the Superfund Basic Research Program for the past year, has departed from CRIS. He chose to remain in North Carolina, accepting a position at the EPA.

Mr. Rodney Winchel, a Presidential Management Intern (PMI) appointed to the Office of the Director/ National Institutes of Health (OD/NIH), has left the NIEHS Worker Education and Training Program to continue his PMI rotation with the Intramural Administrative Management Branch for the Division of Intramural Research at the National Institute of Allergy and Infectious Disease.